

Preserving Renal Function in Surgical Patients

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Postoperative acute renal failure, especially associated with oliguria, carries a high rate of mortality and morbidity. This complication can frequently be avoided if physicians are knowledgeable about preventable or modifiable risk factors. Patients who have underlying renal disease, sepsis, volume depletion or other conditions associated with renal hypoperfusion, or who have severe liver disease, are at particular risk. Exposure to nephrotoxic agents and wide fluctuations of intravascular volume are key conditions that can usually be minimized. Managing patients with chronic advanced renal failure (creatinine clearance 10 to 25 ml per minute) requires close interaction between the internists, anesthesiologists and surgeons. Understanding associated metabolic and organ system disorders is necessary to prevent complications and preserve remaining renal function. Chronic renal failure should not be a contraindication to an elective or emergent surgical procedure.

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Mortality in patients in whom acute oliguric renal failure develops postoperatively has remained greater than 50% over the past 30 years despite advances in supportive care,^{1,2} due in part to the development of more complex surgical procedures and more frequent surgical treatment of high-risk patients. The underlying reason for an operation and the overall health of a patient also determine the outcome. Though dialysis has decreased mortality in patients with postoperative acute renal failure³ and total parenteral nutrition appears to be of value in their support,⁴ the statistics remain grim. Nonoliguric renal failure, usually resulting from nephrotoxic agents or ischemia, carries a more benign prognosis, with mortality rates ranging from 7% to 26%.^{5,6} Nevertheless, prevention is preferable, and determining which patients are susceptible to renal failure before a surgical procedure allows a physician to correct reversible conditions and anticipate potential problems.

Patients with chronic advanced renal failure (creatinine clearance 10 to 25 ml per minute) frequently have extrarenal manifestations of their renal dysfunction that could complicate a procedure and are at high risk for fluid, electrolyte and drug imbalance.

The prevention of acute renal failure and the care of surgical patients with established renal failure require the close cooperation of internists, surgeons and anesthesiologists. Patients already receiving hemodialysis should be followed by a nephrologist. In this article, we discuss the evaluation of renal function in surgical patients, the prevention of acute postoperative renal failure and the management of patients following an operation who have established renal disease and who are not yet receiving dialysis.

Evaluating Renal Function in Surgical Patients

Preexisting renal disease is thought to increase the risk of postoperative decline of renal function. As patients with significant renal disease may be asymptomatic, preoperative screening for renal function is mandatory. A urinalysis is

useful to discover renal abnormalities. An inappropriately low specific gravity may hint at tubular dysfunction. The presence of hemoglobin on a dipstick examination may indicate hemoglobinuria or myoglobinuria, with their attendant risks of renal failure. The presence of erythrocytes, erythrocyte casts, leukocytes, leukocyte casts or bacteria may suggest glomerulitis, vasculitis or infection. Because urinary infection can be a source of graft or prosthesis infection or sepsis and can impair renal function in patients with underlying renal disease, it should be adequately treated before an elective operation. The blood urea nitrogen level is affected by volume status, urine flow and protein intake and is not a reliable indicator of renal function. The serum creatinine value is more accurate, though it does vary directly with muscle mass and also may be disproportionately elevated in patients with major muscle trauma.⁷ The glomerular filtration rate (GFR) declines with age, but so does muscle mass. Therefore, while a serum creatinine level of 1 mg per dl may reflect a creatinine clearance of 120 ml per minute in a normal 20-year-old patient, it usually reflects a creatinine clearance of only 60 ml per minute in an 80-year-old person with the muscle wasting of normal aging. In pregnancy the serum creatinine level decreases due to a physiologic increase in the GFR with a constant production of creatinine. Thus, serum creatinine values considered normal in nongravid women may indicate renal insufficiency in pregnancy. Creatinine clearance can be a reliable test of renal function, but requires several hours of accurate urine collection. A quick estimate of the glomerular filtration rate may be obtained by the following formula: creatinine clearance = $(140 - \text{age}) \times (\text{weight in kg}) / 72 \times \text{serum creatinine level (mg per dl)}$.⁸ The accuracy of this estimate depends on stable renal function and a normal relationship between weight and muscle mass. For example, patients with significant obesity or ascites excrete less creatinine per kilogram total body weight than expected. In these patients the use of an ideal predicted body weight is recommended.

Preventing Acute Postoperative Renal Failure

Table 1 lists major risk factors for postoperative acute renal failure.

Fluid Balance

Oliguria may reflect intravascular volume depletion, hypotension, decreased cardiac output, obstruction or intrinsic renal disease. Surgical patients should have frequent monitoring of fluid intake and output, postural vital signs and prompt replacement of fluid losses. In a patient with oliguria (less than 500 ml per 24 hours of urine output), obstruction is most readily ruled out by catheterizing the bladder and doing a sonogram of the kidneys and ureters. In the absence of obstruction, a high urine specific gravity and low urine sodium level suggest prerenal causes. Other, more sophisticated indices of renal failure such as the fractional excretion of sodium and urine-to-plasma creatinine ratio may be helpful to distinguish prerenal from renal azotemia.⁹

For patients at high risk of postoperative renal failure, some authors recommend the prophylactic preoperative use of diuretics,¹⁰ though this is controversial. There are no large prospective trials establishing a role for the use of mannitol or furosemide in preventing renal failure, and it is unclear whether diuretics offer advantages over volume repletion in preventing acute renal failure. Certain case reports and clinical trials support the beneficial effect of mannitol in surgical procedures with high risk of renal failure such as open heart,¹¹ complicated biliary¹² and major vascular operations.¹³ Other clinical studies in similar settings have not found mannitol to be of benefit.^{14,15} Also controversial is whether administering diuretics reverses incipient oliguric

TABLE 1.—Risk Factors for Postoperative Acute Renal Failure

Preoperative Risk Factors
Preexisting renal disease
Volume depletion
Decreased effective blood volume
Congestive heart failure
Nephrotic syndrome
Cirrhosis
Hypotension
Volume depletion due to disease state
Burns
Trauma
Gastrointestinal bleeding
Pancreatitis
Acute surgical abdomen
Vomiting
Osmotic diuresis (glucose, urea)
Volume depletion due to iatrogenic causes
Diuretics
Fasting
Osmotic diuresis (mannitol, contrast dye studies)
Bowel preparations
Nasogastric suction
Nephrotoxic agents
Exogenous—drugs, contrast dyes
Endogenous—hemoglobin, myoglobin
Obstructive jaundice
Intraoperative Risk Factors
Anesthesia
Cardiopulmonary bypass
Postoperative Risk Factors
Infection—systemic, intra-abdominal

TABLE 2.—Proposed Uses of Mannitol and Furosemide

In patients with crush injuries, hemolysis, acute uric acid loads
Fluids given intravenously
Mannitol or furosemide given to maintain urinary flow rates of 2 to 4 liters a day for 2 to 3 days.
In patients with nonobstructive postoperative oliguria
Fluids given intravenously until a patient is euvoletic
If still oliguric, a trial of mannitol (12 to 25 grams) or furosemide (80 to 320 mg) given intravenously

renal failure. Clinical studies on the benefit of furosemide in established renal failure have come to opposite conclusions, some showing benefit and others not.¹⁶ Similarly, the beneficial effect of diuretics in patients with crush injuries has not been firmly established. In this controversial area, it seems reasonable to follow the practical advice of Levinsky and co-workers as outlined in Table 2.¹⁷ When using these agents, care must be taken to avoid volume depletion. Patients who receive mannitol without response should be assessed for signs of volume overload as this hypertonic drug will draw fluid into the intravascular space.

In addition to hydration and diuretics in patients with crush injuries, alkalinizing the urine with the use of sodium bicarbonate has been recommended to enhance the rate of excretion of myoglobin and minimize its toxicity.¹⁸ The efficacy of the use of bicarbonate remains controversial, however.¹⁹ Large doses may fail to alkalinize the urine, and alkalemia, if achieved, could theoretically enhance deposition of calcium salts into muscle, leading to tetany.

Nephrotoxins

Because there are excellent reviews of agents known to cause renal failure,^{20,21} only a few examples most pertinent to surgical patients will be discussed here.

Radiocontrast dye. The incidence of radiocontrast dye-induced nephropathy is unknown. Most experts agree that patients at increased risk of this complication include the elderly, those with preexisting renal disease or volume depletion or patients exposed to repeated doses of contrast over a short time interval.²² The underlying reason for an operation and overall health of a patient also determine outcome. Although diabetes mellitus has been held to be a risk factor for dye-induced renal failure, recent work suggests that most nonazotemic patients with diabetes have no significant renal decline after contrast has been given,²³ though diabetic persons with renal insufficiency (creatinine level greater than 2 mg per dl) are clearly at high risk.²⁴ In these vulnerable patients, procedures that do not use dye, such as ultrasound, should be used if at all possible. If more than one dye study is required, they should be scheduled as far apart as possible. Hypovolemia should be avoided by limiting preparatory fluid restriction or laxative use, and, in fact, hydration with a saline solution given intravenously for several hours before the procedure is frequently indicated to ensure adequate intravascular volume and renal perfusion. Because contrast agents produce an osmotic diuresis, the urine output should be monitored and volume loss replaced after the procedure. The serum creatinine level should be measured 24 to 48 hours after the procedure to screen for contrast nephropathy.

Aminoglycosides. The incidence of aminoglycoside nephrotoxicity is recently reported to be from 8% to 26%.²⁵ It usually presents as nonoliguric renal failure about five to seven days after initiation of the drug regimen. Often the renal

failure is mild and reverses with discontinuation of the therapy. Patients getting aminoglycosides are frequently of advanced age or have prior renal disease or volume depletion or are concurrently using other nephrotoxic drugs. The relative importance and potential for interaction of these factors has not been established.²⁰ The presence of hypotension or sodium depletion enhances aminoglycoside toxicity in animals and may do so in humans. Furosemide, in the absence of volume depletion, probably does not potentiate aminoglycoside renal failure, but furosemide and aminoglycosides are both ototoxic. This is of particular concern in elderly patients in whom some degree of eighth nerve compromise may already exist. The combination of cephalothin and aminoglycoside may be more nephrotoxic than penicillin and aminoglycoside,²⁶ and though there are insufficient data on the newer generation cephalosporins, it would seem prudent to avoid the cephalosporin-aminoglycoside combination if possible in high-risk patients. Liver disease has recently been shown to be a risk factor for aminoglycoside renal failure.²⁷ Because elevated peak and trough aminoglycoside levels are associated with renal toxicity, all patients should have these measured on the third day and monitored, along with serum creatinine levels, thereafter.

Nonsteroidal anti-inflammatory drugs. The physiologic effects of renal prostaglandins remain incompletely defined.²⁸ They appear to antagonize the vasoconstrictive effects of angiotensin or norepinephrine released during renal ischemia, thus maintaining renal blood flow and the GFR. Nonsteroidal anti-inflammatory drugs, by blocking prostaglandin-mediated vasodilatation, lead to unopposed renal vasoconstriction, hypoperfusion and a decreased GFR. These drugs may cause a reversible decrease in renal function when given to patients with volume depletion, intrinsic renal disease, congestive heart failure, the nephrotic syndrome or cirrhosis.²⁸ They should not be used in surgical patients with renal disease or the potential for renal ischemia. To minimize the risk of renal injury, it may be prudent to discontinue the use of these agents in all patients a few days before a nonemergency operation.

Obstructive Jaundice

For uncertain reasons, patients with obstructive jaundice preoperatively are at high risk for having postsurgical renal failure and complications not seen in nonjaundiced patients who have postoperative renal failure.¹⁰ Uremia aggravates the complications of obstructive liver disease by increasing the pool of urea available for degradation to ammonia in the gut, increasing bleeding due to functionally inactive platelets and increasing the risk of infection. In these patients renal failure may cause the bilirubin level to rise to a level deleterious to body tissues. Because surgical intervention is often required in a patient with obstructive jaundice, scrupulous attention to renal function is required.

Anesthesia

All general anesthetics appear to decrease renal blood flow in proportion to the depth of anesthesia.²⁸ Spinal anesthesia in humans causes only a slight change in renal blood flow and renal vascular resistance.²⁹ The general anesthetic methoxyflurane is inherently nephrotoxic, as its metabolite fluoride may induce a nephrogenic diabetes insipidus and renal failure.³⁰ Methoxyflurane toxicity is in part dose-related and may be potentiated by the use of phenobarbital, aminoglycosides and tetracycline. Enflurane also produces fluoride as a metab-

TABLE 3.—*Guidelines for Drug Therapy in Patients With Renal Failure*

Use a drug only if specifically indicated
Select a drug with the least renal excretion
Refer to published dosing guidelines for renally excreted drugs
Observe blood concentrations if available and known to be accurate
Check medication list if an adverse reaction of any kind develops
Realize that hepatic dysfunction may decrease a drug's excretion by an alternate route

olite and can induce a diabetes insipidus-like state.³¹ It would be prudent to avoid administering this drug to patients with preexisting renal disease or a prior history of methoxyflurane renal toxicity.

Cardiopulmonary Bypass

A cardiopulmonary bypass operation decreases the GFR by about 30% and the renal plasma flow by 25%.³² This decrease in renal function results from the combined effects of anesthesia, hypothermia, decreased mean arterial pressure, metabolic acidosis and nonpulsatile blood flow. Erythrocytes damaged by the bypass machine release vasoconstrictor substances. The most important risk factor for renal failure may be the duration of extracorporeal circulation.

Infection

Uncontrolled local or systemic infection predisposes surgical patients to renal failure,³³ a result of associated hypotension, vasoconstriction, disseminated intravascular coagulation and nephrotoxic antibiotic therapy.

Caring for Surgical Patients Who Have Advanced Renal Disease

Patients with advanced renal failure (creatinine clearance of 10 to 25 ml per minute) but who are not yet receiving dialysis are often managed conjointly by their general internist and surgeon. Obviously those factors that predispose to acute renal failure in any surgical patient must be assiduously avoided in this vulnerable population. Accurate mortality statistics for surgical patients in this category are, however, unavailable. To assure the best care, particular attention must be paid to drug use, fluid and electrolyte balances, acid-base status, anemia, metabolic-nutritional state and infection.

Drug Use

Adverse drug reactions are common in patients with advanced renal disease.^{34,35} Drug toxicity may occur when renally excreted drugs such as digoxin or drugs with renally cleared active metabolites such as meperidine (Demerol) hydrochloride are given without adjusting for compromised renal function. Uremia alters the protein binding of certain drugs and thus can affect total and unbound drug concentrations.³⁶ Serum phenytoin levels, for example, are notoriously unreliable in cases of uremia, and patients with "normal" levels in the laboratory may have a toxic reaction. The use of sodium- or potassium-containing antibiotics, innocuous in normal patients, can cause volume overload or hyperkalemia in patients with renal disease. When using drugs in patients with renal failure, following certain principles will minimize complications (Table 3). The level of renal function, estimated by the creatinine clearance (see section on evaluation of renal function), is the basis for calculating drug dosing. A standard initial dose should be given when it is important to

reach a therapeutically effective concentration in the shortest time possible, such as when using antibiotics. Maintenance doses are then adjusted by changing either the dosing interval or the dose of the drug. For drugs excreted entirely by the kidneys, either of the following formulas can be used as an initial guide. Because no controlled clinical trials have been done to establish their comparative efficacy or toxicity, the choice of methods depends primarily on which gives the more convenient dose or administration schedule.³⁷

Dosing interval for patients with renal failure:

Normal dosing interval \times (normal creatinine clearance/patient's creatinine clearance).

Dose for patients with renal failure:

Normal dose \times (patient's creatinine clearance/normal creatinine clearance).

Dosing guidelines for many drugs are readily available in the literature.³⁸

Fluid Balance

A common cause of deteriorating renal function in surgical patients with renal disease is fluid depletion. Volume deficiency may not be evident on physical examination and measuring urine and serum sodium levels is not always helpful, as they may be either high or low in these patients. A fluid challenge may be warranted, and consideration should be given to measuring through a Swan-Ganz catheter in patients whose volume status is uncertain. Decreasing renal function may also signal the presence of congestive heart failure, and because this is a major surgical risk factor,³⁹ nonemergency surgical procedures should be postponed for several days until a patient is treated with appropriate drugs or dialysis.

Preoperative hypertension usually results from fluid overload and responds to diuresis with a potent drug such as furosemide. Thiazides are ineffective in patients with a creatinine clearance of less than 30 ml per minute, and potassium-sparing diuretics such as triamterene are both ineffective and associated with the risk of serious hyperkalemia. When therapy with a second drug is indicated, hydralazine hydrochloride is particularly useful because it has a rapid onset and

can be given parenterally. The data of Goldman and Caldera⁴⁰ suggest that no benefit accrues from postponing an operation solely to control the blood pressure in patients whose diastolic blood pressure is less than 110 mm of mercury. Patients with underlying hypertension remain at about 25% risk of intraoperative hypertension or hypotension even with preoperative normalization of blood pressure. It is safe and desirable to continue a patient's regular antihypertensive medication regimen up to and including the morning of a procedure and resume it immediately after the operation.⁴¹

Intraoperative hypotension occurs mostly in patients who are dialyzed, with fluid removal, less than 24 hours before an operation, who are receiving antihypertensive drugs or who have a kidney removed that was a major source of preoperative hypertension. Swan-Ganz monitoring intraoperatively of such unstable patients is warranted.

Hypertension or congestive heart failure (or both) may develop during the second or third postoperative day as fluid is mobilized intravascularly from interstitial tissues. It should be watched for and vigorously treated, principally with diuretics.

Electrolyte Balance

Hyponatremia occurs commonly in patients with renal disease and can be due to a variety of disorders. Because treatment varies significantly, it is important to determine a cause (Figure 1). The first step is to calculate or measure serum osmolality. A simple calculation is $2(\text{serum sodium} + \text{potassium}) + (\text{serum urea}/2.8) + (\text{serum glucose}/18)$. Hyponatremia, with normal or high serum osmolality, may be due to hyperlipidemia, hyperglycemia or hyperproteinemia. Other hyponatremic conditions are associated with hypotonicity, where the total body water level is inappropriately high with respect to the total body sodium level. The extracellular fluid volume should be clinically assessed in these patients with vital signs, intake and output records, skin turgor and neck veins. The usual laboratory tests of volume may be difficult to interpret in patients with renal disease whose serum hematocrit is usually decreased, urea and creatinine concentrations increased and ability to concentrate urine impaired.

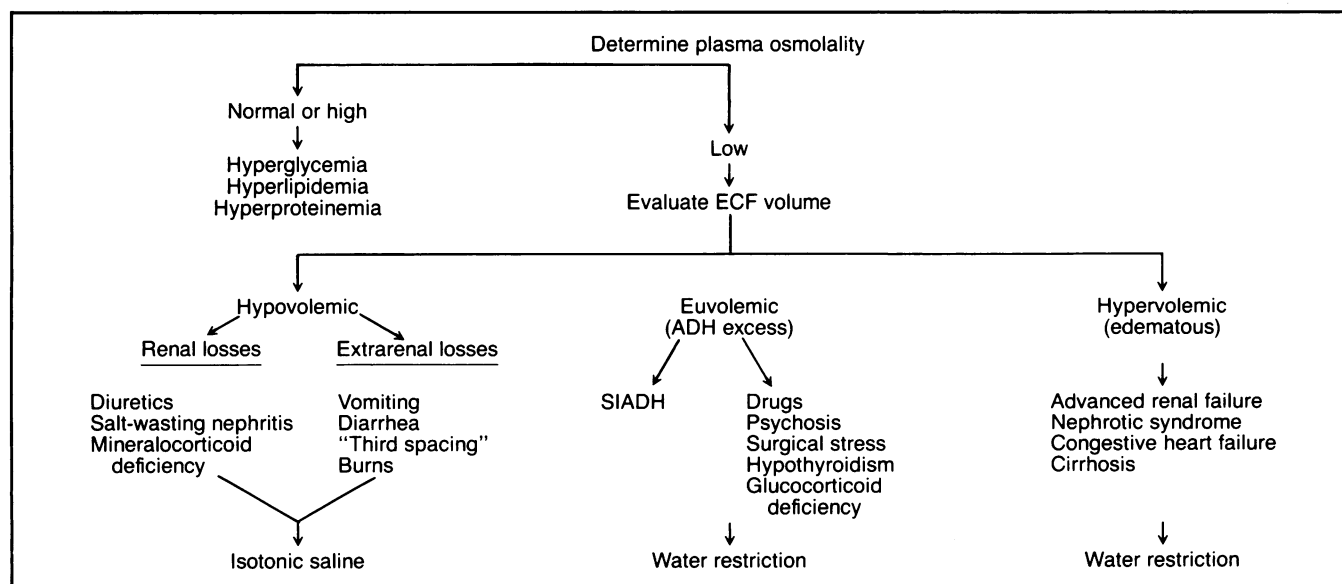


Figure 1.—Diagnostic approach to hyponatremia. ADH = antidiuretic hormone, ECF = extracellular fluid, SIADH = syndrome of inappropriate [excretion of] ADH

In patients with renal failure, hyponatremia is usually associated with excess total body sodium levels because the ability to excrete free water diminishes as the kidneys fail. This may be exacerbated by a surgically stimulated release of pituitary antidiuretic hormone.⁴² Restricting free water will correct hypervolemic hyponatremia. Hyponatremia associated with volume depletion can develop in a patient with renal failure due to any factor that causes a proportionately greater loss of sodium than water, including overzealous diuretic use, vomiting, diarrhea, "third spacing" or osmotic diuresis from the use of mannitol, urea or glucose. This is compounded by a diseased kidney's inability to rapidly decrease sodium excretion. Patients with a GFR of 10 to 15 ml per minute whose sodium intake is severely restricted may be unable to reduce sodium excretion to equal the sodium intake even after two to three weeks. In surgical patients euvoletic hyponatremia usually results from excessive use of hypotonic fluids and antidiuretic hormone excess from drugs, surgical stress or the syndrome of inappropriate antidiuretic hormone excretion. Restricting free water is the treatment of choice. To avoid central nervous system complications, it is prudent to treat all patients whose serum sodium level is less than 125 mEq per liter. It is recommended that the preoperative level be raised to a minimum of 131 mEq per liter.⁴³

Many factors cause hyperkalemia in surgical patients with renal disease (Table 4). Hyperkalemia may develop intraoperatively if patients are not hyperventilated to maintain their habitual respiratory compensation for underlying metabolic acidosis, or postoperatively if their endotracheal tube is removed too soon or if they are kept heavily sedated. Hyperkalemia is a risk factor for postoperative death from ventricular arrhythmias,⁴⁴ and it is important to lower the serum potassium level to less than 5 mEq per liter before a surgical procedure to give a safe margin for a possible rise in the potassium level during the intraoperative or immediate postoperative period. In urgent situations (serum potassium level greater than 7.5 mEq per liter or electrocardiographic changes of hyperkalemia), a regimen of calcium gluconate, insulin plus glucose or sodium bicarbonate given intravenously lowers potassium levels immediately for one to two hours. A cation-exchange resin (sodium polystyrene sulfonate [Kayexalate]) given orally or rectally works more slowly but removes potassium from the body. Kayexalate exchanges sodium for potassium so should be used with caution in patients

at risk for volume overload. Hemodialysis is an effective definitive treatment when the above measures cannot be used. Preoperative hypokalemia in these patients is less common, but should it occur, replacement must be given slowly and monitored carefully with serum potassium levels measured frequently.

Metabolic Acidosis

Metabolic acidosis, common in renal failure, predisposes patients to arrhythmias during an operation. Surgical patients may suffer superimposed lactic acidosis, ketoacidosis or the loss of their compensatory hyperventilation as described. In these patients, the serum bicarbonate level may drop to as low as 5 mEq per liter. Any reversible process should be identified and corrected, and the serum bicarbonate level should be raised to 15 mEq per liter; levels above this add very little to the physiologic function.⁴⁴ This can be done using the following formula as a guide: mEq of sodium bicarbonate required = $0.5 \times \text{total body weight in kg} \times (15 - \text{bicarbonate measured})$. If a patient with acidosis has volume overload or hypernatremia, dialysis is indicated.

Anemia

Patients with chronic renal failure are generally well adapted to their anemia, and presurgical transfusions are usually unnecessary.^{45,46} Patients with less than 7 to 8 grams of hemoglobin who are elderly or have coronary artery disease may be symptomatic and benefit from transfusions. To minimize volume overload and hyperkalemia, transfusions should be with fresh or fresh-frozen packed erythrocytes. Patients who are euvoletic before a transfusion should be given furosemide intravenously with each transfusion to avoid precipitating congestive heart failure.

Hypercatabolism

Disorders requiring a surgical procedure and the procedure itself induce a catabolic state that quickly becomes apparent in patients with limited renal reserve. The potential for malnutrition due to restricted "renal failure" diets, increased metabolic needs and gastrointestinal dysfunction must be anticipated. Clinical surgical experience suggests that parenteral nutrition can reduce complications and improve survival in selected surgical patients.⁴⁷

Infection

Infection occurs in as many as 32% of surgical patients with renal failure,^{45,46} often with significant prolongation of the hospital stay. The lungs, the wound and the genitourinary tract remain the most frequent sites, and infection of the genitourinary tract may cause further deterioration of renal function by inflammation or functional obstruction. Infection should be aggressively prevented, with emphasis given to nutritional support, early ambulation, scrupulous pulmonary toilet and minimizing the use of invasive instruments, especially urethral catheters. No data exist proving the efficacy of routine antibiotic prophylaxis solely for renal failure, and this practice is not recommended.

Summary

Patients in whom acute postoperative renal failure develops have a high mortality despite progress in supportive therapy. The most effective method of prevention is to recog-

TABLE 4.—Common Causes of Hyperkalemia in Surgical Patients With Chronic Renal Failure

<i>Exogenous</i>
Total parenteral nutrition
Potassium supplements
"Co-salt" (salt substitute containing potassium chloride)
Blood transfusion
Potassium-containing drugs, including antibiotics
Respiratory depressants that compromise compensatory hyperventilation
<i>Endogenous</i>
Hemolysis
Reabsorption of hematoma
Rhabdomyolysis
Tissue trauma
Metabolic acidosis
Cell-membrane depolarizing drugs, such as succinylcholine chloride
Failure to appropriately hyperventilate

nize and modify, if possible, any predisposing factors. General internists, surgeons and anesthesiologists must also deal with patients who have established renal failure. These surgical patients often have many associated medical problems and tenuously balanced metabolism. Awareness of frequently occurring problems and conditions that lead to worsening renal failure in surgical patients will minimize complications and preserve the remaining renal function.

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